Appl. No. 10/556,901

Atty. Dkt.: 620-401

Amendment After Final Rejection

March 20, 2008

AMENDMENTS TO THE CLAIMS:

Please amend the claims as follows:

1. (Withdrawn – Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 34 formula I, or a pharmaceutically acceptable salt thereof:

wherein

X is CH;

R⁴ is H, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or –NH₂; or C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or –NH₂; or –OR, –NHR, –NR₂ or –SR wherein R is C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or –NH₂;

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 R^2 is H, CF_3 ; or optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl, C_{5-7} heterocyclyl or together with R^3 an optionally substituted C_{3-4} alkylene group wherein L^3 and L^4 are single bonds thus forming a C_{5-6} ring fused with the aromatic ring to which L^3 and L^4 are attached;

 R^3 is H; or optionally substituted $C_{5\cdot6}$ aryl, $C_{3\cdot7}$ cycloalkyl, $C_{5\cdot7}$ heterocyclyl or together with R^2 an optionally substituted $C_{3\cdot4}$ alkylene group wherein L^3 and L^4 are single bonds thus forming a $C_{5\cdot6}$ ring fused with the aromatic ring to which L^3 and L^4 are attached;

R⁴ is H; or optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl;

R⁶-is selected from H or optionally substituted C₁₋₇ alkyl, C₅₋₆ aryl and C₁₋₄ alkylene-C₅₋₆ aryl;

 L^4 is optionally substituted C_{5-6} arylene, C_{1-4} alkylene C_{5-6} arylene or $-L^5N(R^5)L^6$, or C_{1-4} alkylene substituted by either C_{1-7} alkyl or C_{5-7} aryl, wherein L^5 and L^6 are independently selected from optionally substituted C_{1-4} alkylene and C_{5-6} arylene, and R^5 is H or C_{1-4} alkyl; and further wherein L^4 may be unsubstituted C_{1-4} alkylene when X is N;

L² is a single bond; and

L³-and L⁴-are independently selected from a single bond, optionally substituted C₁₋₄ alkylene, -L⁹YN(OH)C(=O)L¹⁰- and -L⁹C(=O)N(OH)YL¹⁰-, wherein L⁰- and L¹⁰- are

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independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene C_{5-6} arylene and a single bond, wherein Y is NH or a single bond.

- 2. (Withdrawn Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 37A method according to claim 1 wherein R¹ is chosen from the group consisting of H and cyano.
- 3. (Withdrawn Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 38A method according to claim 1 wherein R⁶ is H or C₁₋₇ alkyl.
- 4. (Withdrawn Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 39A method according to claim 1 wherein L¹ is chosen from the group consisting of phenylene, -CH(Ph)-, -CH₂-phenylene- and -CH₂C(=O)NH-phenylene-.

Claim 5. (Canceled)

6. (Withdrawn – Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 39A method according to claim 1 wherein L³ is chosen from the group consisting of a single bond, –

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L⁹YN(OH)C(=O)L¹⁰- and -L⁹C(=O)N(OH)YL¹⁰-, wherein L⁹ and L¹⁰ are independently selected from optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene, C₁₋₄ alkylene-C₅₋₆ arylene and a single bond, and wherein Y is NH or a single bond.

- 7. (Withdrawn Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 44. A method according to claim 6 wherein L³ is a single bond.
- 8. (Withdrawn Currently Amended) A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 45. A method according to claim 1 wherein L⁴ is chosen from the group consisting of a single bond, L⁹YN(OH)C(=O)L¹⁰ and –L⁹C(=O)N(OH)YL¹⁰ –, wherein L⁹ and L¹⁰ are independently selected from optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene, C₁₋₄ alkylene-C₅₋₆ arylene and a single bond, and wherein Y is NH or a single bond.
- 9. (Withdrawn Currently Amended) <u>A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound of claim 46A method according to claim 8 wherein L⁴ is selected from the group consisting of CH₂N(OH)C(=O)-, -phenylene-CH₂N(OH)C(=O)-, -phenylene-NHN(OH)C(=O)- and -CH₂C(=O)N(OH)-.</u>

Claim 10. (Canceled)

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11. (Withdrawn – Currently Amended) A method of treating a condition which

can be alleviated by inhibition of glyoxalase I, which method comprises administering to

a patient in need of treatment an effective amount of a compound of claim 47A method

according to claim 1 wherein one of R⁴. R² and R⁴ are H.

12. (Withdrawn – Currently Amended) A method of treating a condition which

can be alleviated by inhibition of glyoxalase I, which method comprises administering to

a patient in need of treatment an effective amount of a compound of claim 48A method

according to claim 1 wherein two of R¹, R² and R⁴ are H.

Claims 13-20. (Canceled)

Claim 21. (Canceled)

Claims 22-29. (Canceled)

Claim 30. (Canceled)

31. (Previously Presented) A pharmaceutical composition comprising a

compound according to claim 34 or a pharmaceutically acceptable salt thereof together

with a pharmaceutically acceptable carrier or diluent.

Claims 32-33. (Cancelled)

34. (Currently Amended) A compound of formula I:

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or a salt, solvate or chemically protected form thereof wherein

X is CH;

R¹, R² and R⁴ are [[is]] H;, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or – NH₂; or C₁₋₄-alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or – NH₂; or – OR, – NHR, – NR₂ or – SR wherein R is C₁₋₄-alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or – NH₂;

 R^2 is H, CF_3 ; or optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl, C_{5-7} heterocyclyl or together with R^3 an optionally substituted C_{3-4} alkylene group wherein L^3 and L^4 are single bonds thus forming a C_{5-6} ring fused with the aromatic ring to which L^3 and L^4 are attached;

 R^3 is [[H; or]] optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl, <u>or</u> C_{5-7} heterocyclyl or together with R^2 an optionally substituted C_{3-4} alkylene group wherein L^3 and L^4 are single bonds thus forming a C_{5-6} ring fused with the aromatic ring to which L^3 and L^4 are attached:

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R⁴ is H; or optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl;

 R^6 is selected from H or optionally substituted C_{1-7} alkyl, C_{5-6} aryl and C_{1-4} alkylene- C_{5-6} aryl;

 L^{1} is optionally substituted [[C₁₋₄ alkylene,]] C₅₋₆ arylene, C₁₋₄ alkylene-C₅₋₆ arylene or $-L^{5}N(R^{5})L^{6}$ -, or C₁₋₄ alkylene substituted by either C₁₋₇ alkyl or C₅₋₇ aryl, wherein L^{5} and L^{6} are independently selected from optionally substituted C₁₋₄ alkylene and C₅₋₆ arylene, and R^{5} is H or C₁₋₄ alkyl;

L² is a single bond; and

L³ is a single bond; and

 L^4 [[are]]is independently selected from a single bond, optionally substituted C_{1-4} alkylene, $-L^9$ YN(OH)C(=O) L^{10} - and $-L^9$ C(=O)N(OH)Y L^{10} -, wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, wherein Y is NH or a single bond; and

wherein the compound contains at least one -C(=O)N(OH)- group.

Claims 35-36. (Canceled)

- 37. (Previously Presented) A compound according to claim 34 wherein L^4 is a L^9 –C(=O)N(OH)- group.
 - 38. (Original) A compound according to claim 37 wherein L⁹ is selected from C₁₋₄

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alkylene and C_{5-6} arylene.

39. (Original) A compound according to claim 37 wherein L⁹ is methylene or phenylene.

Claim 40. (Canceled)

Claims 41-43. (Canceled)

- 44. (Previously Presented) A compound according to claim 34 wherein \mathbb{R}^3 is optionally substituted \mathbb{C}_{5-6} aryl.
 - 45. (Original) A compound according to claim 44 wherein R³ is phenyl.
- 46. (Previously Presented) A compound according to claim 34 wherein R^6 is H or C_{1-7} alkyl.
 - 47. (Original) A compound according to claim 46 wherein R⁶ is H or C₁₋₃ alkyl.
- 48. (Previously Presented) A compound according to claim 34 wherein L¹ is phenylene, -CH(Ph)-, -CH₂-phenylene- or -CH₂C(=O)NH-phenylene-.

Claim 49. (Canceled)

Claim 50. (Canceled)